REMARKS

The Official Action dated October 27, 2010 has been carefully considered. Accordingly, the present Amendment is believed sufficient to place the present application in condition for allowance. Reconsideration is respectfully requested.

By the present amendment, claims 1, 12 and 23 are amended to clarify that the output data matrix represents the red blood cell concentration of the microcirculation, support for which may be found throughout the present application, for example at page 8, first paragraph, page 9, first full paragraph, and Figs. 2 and 3, including their descriptions at page 11. Claims 12, 13, 36 and 38 are also amended to correct typographical errors. It is believed that these changes do not involve any introduction of new matter, whereby entry of the amendments is in order and is respectfully requested.

In the Official Action, claims 12, 14 and 15 were rejected under 35 U.S.C. §103(a) as being unpatentable over the Shih U.S. Patent No. 6,061,176 in view of the Godik U.S. Patent No. 5,699,797, the Nilsson U.S. Patent No. 5,361,769 and the Zinser et al U.S. Patent No. 5,620,000. The Examiner asserted that Shih discloses a microscope for determining microcirculation of blood and including a white light source such as a flash light 18, dual-optical-circuit monochromatic light sources 17 comprising a high color temperature bromine-tungsten lamp 171 and a high-pressure mercury-vapor lamp 172, a scan, track and auto digits display system 10, a detector 110, a pick-up tube 112, an optical index plate 113, and two spectral prisms. The Examiner admitted that Shih does not mention data matrixes representing red, blue and green and displaying or presenting microcirculation in red, green and blue and the use of a polarized filter. However, the Examiner asserted that Shih discloses stacked signals to digital graph

signals and images of microcirculation with stack graphs are displayed on the monitor 5, and Zinser et al teach a polarizing filter that is capable of illuminating a tissue surface with polarized light. The Examiner relied on Nilsson as disclosing a photodetector 9 detecting backscattered light from a body part into a signal processing unit and delivering measurement values to a computer 7 to determine blood circulation, along with a color monitor to display microcirculation in specific colors. The Examiner relied on Godik as disclosing display microcirculation behaviors of physiological liquids marked with the help of pseudo-colors which could be red, green, and blue. The Examiner asserted it would have been obvious to combine Shih with Godik and Nilsson to use pseudo colors and specific colors which could be red, green and blue and to combine Shih with Zinser by using a polarizing filter and computer that separates data into matrixes that could be red, green and blue.

Claims 13 and 20-22 were rejected under 35 U.S.C. §103(a) as being unpatentable over the previous combination in view of the Crutchfield et al U.S. Publication No. 2002/0091320, claims 16-18 and 36-38 were rejected under 35 U.S.C. §103(a) as being unpatentable over the previous combination in view of the Nakakuki U.S. Publication No. 2004/0208393, and claim 19 was rejected under 35 U.S.C. §103(a) as being unpatentable over the previous combination in view of the Takahashi et al U.S. Patent No. 4,366,529. The Examiner relied on Crutchfield et al as teaching a system having the capability for a variety of communication mechanisms such as access to the Internet, administering vasoactive drug, and color codes to display blood flow characteristics, on Nakakuki as teaching that image data corresponding to red, green and blue may be divided into a group of pixels in a matrix and the luminance for each pixel may be represented as 8-bit data and converted into a numerical value on a scale, and on Takahashi et al

as teaching the use of optical fibers to direct an illuminating light beam to a portion of a body cavity.

These rejections are traversed and reconsideration is respectfully requested. More particularly, according to claim 12, the system for determining microcirculation of a living tissue according to the present invention comprises (i) a white light source and a filter capable of illuminating a tissue surface with polarized light, (ii) a polarizing filter for collecting backscattered light; (iii) a photosensitive array capable of detecting the backscattered and polarized light and converting the detected light to a collected information of digital values; and (iv) a computing device receiving said collected information and adapted to separate it into data matrixes representing red, blue and green colors, respectively, and to employ an algorithm using the data matrixes to generate an output data matrix representing the red blood cell concentration of the microcirculation.

Thus, the presently claimed system determines microcirculation based on the concentration of red blood cells. As explained in the specification, for example at pages 8-9, "red" photons have a tendency to be less absorbed by the red blood cells than "green" and "blue" photons, and, consequently, the more red blood cells in the tissue, indicative of a higher degree of vasodilatation, the higher is the absorption of "green" and "blue" photons in relation to the absorption of "red" photons in the polarized white light which reaches the tissue surface. The photosensitive array detects the backscattered and polarized light, indicative of the degrees of absorption of the respective photons, and converts the detected light to a collected information of digital values. The computing device is adapted to separate the collected information into data matrixes representing red, blue and green colors, respectively, and to employ an algorithm using

the data matrixes to generate an output data matrix representing the red blood cell concentration of the microcirculation. Importantly, the digital values are separated into the red, blue and green data matrixes which are then used to generate the output data matrix the values of the output data matrix relate linearly to the red blood cell concentration at each pixel. This output data matrix may then be presented, for example, as a color-coded pseudo image on a computer monitor using a color scale ranging from blue (low red blood cell concentration) to red (high blood cell concentration).

There are at least four novel features of the system defined by claim 12. First, the operability of the computer to use the three matrixes in an algorithm to form the output data matrix representing the red blood cell concentration of the microcirculation solves the problem of adverse effects from fluctuating light intensity from the illuminating device. In one embodiment, a combination of the values of the red and green matrixes are normalized by the blue matrix (see Fig. 5, (R-G)/B), although the algorithm can take various forms. Since the values of the red, green and blue matrixes are linearly related to the illuminating light intensity, this makes the values of the output data matrix independent of the illumination light intensity and related only to the spectral signature. The claimed computer operability using an algorithm based on a principle that eliminates the adverse effects of alterations in the illumination is neither taught nor suggested by the cited prior art.

Second, the combination of this ability to eliminate fluctuations in illuminating light intensity on the output data matrix and the use of the polarizing filter further eliminates the effect of direct surface reflections (cross-polarized mode) on the output data matrix. That is, if direct surface reflections are not eliminated by use of a polarizing filter, part of the individual values of

the red, green and blue matrixes will be saturated and the output data matrix will be seriously distorted. Such distortion can easily be seen, for instance, in photos in standard dermatology reference books where part of a photographed object is white due to direct surface reflections. The polarization filter also allows for the detection of images from, on the average, a somewhat deeper depth, thereby giving a more accurate measure of the microcirculation in the entire dermis. The combination of the polarization filter and the algorithm that eliminates the adverse effects of saturation is neither taught nor suggested by the cited prior art.

Third, the combination of a white light source and the polarizing filter which provides wavelength band separation on the detector side is more beneficial than using illumination by different wavelengths at different points in time. That is, rapid alterations in the microcirculation (on a sub-second scale) may not be represented correctly if time has to be allocated to change filters in front of the illuminating device. Consequently, separation of different wavelength bands on the detector-side, combined with polarization and an algorithm that eliminates the adverse effect of illumination light fluctuation, provided by the system of claim 12 eliminates further adverse effects of image distortion. This combination is neither taught nor suggested by the cited prior art.

Fourth, the presentation of an output matrix in terms of a pseudo color image, for example, using a color scale ranging from blue to red, is well-known from, e.g., ultrasonic color Doppler techniques. The use of such a pseudo color scale incorporating red, green and blue colors must, however, not be confused with the use of red, green and blue filters in the detection devise to capture "photos" within these separate wavelength bands, as is provided by the system

of claim 12. This significant difference will be further discussed with respect to the cited prior art.

Thus, an important feature of the system of the present invention is the use of the separated red, green and blue data matrixes in the algorithm to form an output signal that is normalized and thus independent of alterations in the illumination of the object. These alterations can be substantial because of, for example, fluctuations in the flash intensity or the distance between the flash and the object. The combination of the polarization filter and this algorithm further eliminates the saturation of the photo due to direct reflections in the skin surface and thus gives accurate values of the output matrix representing the microcirculation. The cited combinations of references do not, alone or in combination, teach or suggest the system for determining microcirculation as recited in claim 12 or these advantages thereof.

Specifically, Shih describes a scanning microscope system using monochromatic light of two wavelengths for observation of the microcirculation and further video signal presentation on a monitor. Shih discloses that human red blood cells and capillaries have two major wavelengths of absorption spectrum, that is, 4150 Å and 5750 Å, and Shih therefore provides a bromine-tungsten lamp 171 and a mercury-vapor lamp 172 for transmitting light through optical systems having correspondingly arranged multiple layers of medium film filters to produce monochromatic lights having wavelengths of 5800 Å and 4100 Å, respectively. Shih discloses that red blood cells having absorbed these monochromatic lights present a color darker than they usually present while a background basically does not absorb light of these two wavelengths and presents a color lighter than that of the red blood cells.

However, Shih does not disclose the use of a white light source (a broadband source) for observing microcirculation or for representation of microcirculation. While Shih discloses an electronic flashlight 18, this light is employed with a camera 19 as an auxiliary light source to taking instantaneous photographs of microscope displays and not for determining microcirculation as in the presently claimed system. Additionally, Shih does not disclose a computing device adapted to separate collected digital values into data matrixes representing red, blue and green colors and to employ an algorithm, for example based on normalization by dividing the difference of the red and blue matrixes values by the green matrix values, to create an output data matrix that scales linearly with red blood cell concentration and reduces the adverse effects of fluctuating illumination intensity. Nor does Shih teach the placement of a polarizing filter to reduce the adverse effects of direct surface reflections and modulation of measurement depth. Accordingly, the presently claimed system is significantly distinguishable from Shih.

Moreover, the deficiencies of Shih are not resolved by the secondary or tertiary references. For example, Godik discloses a method and apparatus wherein IR radiation emitted from the skin is sequentially recorded by scanning, backscattered light in the visible and near IR regions is recorded, and images from the IR and visible light regions are compared and superimposed (column 3, lines 46-58). Although Godak detects backscattered light by a sensor array following illumination by visible light (which also occurs in an ordinary digital camera), Godak does not teach or suggest a computing device receiving collected information and adapted to separate it into data matrixes representing red, blue and green colors, respectively, and to employ an algorithm to the data matrixes to generate an output data matrix representing the

concentration of red blood cells in the microcirculation, for example by normalization of the data. As discussed above, the ability to apply an algorithm to the data matrixes (by, e.g., dividing the difference of the red and blue matrixes by the green matrix values) creates an output matrix that scales linearly with red blood cell concentration and reduces the adverse effects of fluctuating illumination intensity. Godak provides no teaching or suggestion in this regard. Further, Godak fails to teach a polarizing filter which reduces the adverse effects of direct surface reflections and modulation of measurement depth. Importantly, Applicants find no motivation in Godak to modify any of the teachings of Shih to result in a system as recited in claim 12.

Nilsson is a prior patent of the present co-inventor Nilsson and discloses a system for measuring fluid flow movements, i.e., blood perfusion through tissue, in which a slowly scanning laser beam successively probes tissue point by point for Doppler shifted light caused by dynamic light scattering in moving red blood cells. However, Nilsson does not provide any teaching or suggestion for components to detect or generate different color matrixes, and only one wavelength is used as the laser is highly monochromatic. Thus, Nilsson does not disclose a system having a white light source. Nor does Nilsson disclose a polarizing filter for collecting backscattered light to eliminate surface reflections or to modulate the measurement depth. Further, the "map" generated in the Nilsson system represents local red blood cell velocity with time and concentration (the Doppler principle measures object velocity), whereas the present application generates a "map" of the local tissue red blood cell concentration alone. Using a principle based on the Doppler effect as taught by Nilsson cannot deliver accurate information about the red blood cell concentration, i.e., erythema and blanching or, alternatively,

vasoconstriction or vasodilatation, since the Doppler signal is zero where red blood cells stagnate, even though there may still be a high red blood cell concentration in such tissue. Thus, modification of the Shih teachings in view of Nilsson clearly does not lead to the elements of the present system.

Zinser discloses a method and apparatus wherein a monochromatic scanning light beam (laser) is used to measure the frequency shifted light reflected from movable objects in microcirculation according to the Doppler principle to measure the flow rate (not the concentration) of red blood cells. As with Nilsson, using a principle based on the Doppler effect cannot deliver accurate information about the red blood cell concentration, for example, erythema and blanching or, alternatively, vasoconstriction or vasodilatation, since the Doppler signal is zero where red blood cells stagnate, even though there may still be a high red blood cell concentration in such tissue. Thus, Zinser does not teach the use of simultaneously recorded matrixes of data at different wavebands to calculate the local red blood cell concentration, and therefore, does not provide the modification of Shih necessary to result in the presently claimed system.

Crutchfield discloses a Doppler imaging system using ultrasonic pulses (see paragraph [0064]). One of ordinary skill in the art will appreciate that such an ultrasound system is not relevant to an optical system as presently claimed. Although Crutchfield discloses a variety of communication mechanisms such as access to the Internet, administering vasoactive drug, and color codes to display blood flow characteristics, Crutchfield does not resolve the deficiencies of Shih and, specifically, does not teach a system comprising a white light source, a photosensitive array which detects backscattered and polarized light, indicative of the degrees of absorption of

the respective photons, and converts the detected light to a collected information of digital values, together with a computing device which then separates the collected information into data matrixes representing red, blue and green colors, respectively, and employs an algorithm to the separated matrixes to generate an output data matrix representing the red blood cell concentration of the microcirculation as required by claim 12. Further, Applicants find no apparent reason of record for one of ordinary skill in the art to use any of the Crutchfield teachings to modify the Shih system.

Nakakuki is directed to an image processing device which is adapted to determine if a spectrum of a predetermined physical quantity in image data has a plurality of peaks. An image capturing unit such as a camera is employed. However, Nakakuki is not directed to systems or methods for determining microcirculation and provides no teaching or suggestion of a system for determining microcirculation based on a measured concentration of red blood cells. Importantly, Applicants find no apparent reason of record for one of ordinary skill in the art to use any of the Nakakuki teachings to modify the teachings of Shih, particularly along the lines of the present system.

Finally, Takahashi et al disclose an illumination device for observing and photographing a portion of a body cavity to be examined with an endoscope and including a bundle of optical fibers. However, the Takahashi et al teachings are not directed to systems or methods for determining microcirculation and they provide no teaching or suggestion of a system for determining microcirculation based on a measured concentration of red blood cells. Importantly, Applicants find no apparent reason of record for one of ordinary skill in the art to use any of the

Takahashi et al teachings to modify the system of Shih, particularly along the lines of the present system.

In determining patentability under 35 U.S.C. §103, it is necessary to determine whether there was an apparent reason to combine known elements in the fashion of the claims at issue, *KSR International Co. v. Teleflex, Inc.*, 550 US 398, 418 (2007). Applicants find no evidence of record which would indicate any apparent reason to one of ordinary skill in the art to modify and supplement the teachings of Shih to result in a system as presently claimed which is operable to generate an output data matrix representing the red blood cell concentration of the microcirculation and avoiding adverse effects of illumination and saturation. Thus, the requisite showing that those of ordinary skill in the art would have had some apparent reason to modify the Shih system in a way that would result in the claimed system has not been made.

Accordingly, the system for determining microcirculation according to claim 12, and claims 13-22 and 36-38 dependent thereon, is nonobvious over and patentably distinguishable from the cited combinations of references based on Shih, and the rejections under 35 U.S.C. §103 have been overcome. Reconsideration is respectfully requested.

It is believed that the above represents a complete response to the Official Action and places the present application in condition for allowance. Reconsideration and an early allowance are requested. In the event that the application is not in condition for allowance, the Examiner is encouraged to call the undersigned to resolve any outstanding matters. Please charge any fee required with this response to Deposit Account No. 503915.

Respectfully submitted,
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